REMARKS

The Official Action dated September 14, 2010 has been carefully considered. Accordingly, it is believed that the present Amendment and the Sequence Listings and Statement of Sequence Listing Identity submitted herewith respond fully to the outstanding matters and place this application in condition for allowance. Reconsideration is respectfully requested.

By the present Amendment, the specification is amended to include SEQ ID NOS. Claim 1 is amended to include limitations from claims 2, 3 and 4 and for clarification. Claims 2-4 are cancelled, and claims 5-7, 9-18 and 22-24 are amended to correspond with claim 1 and/or for matters of clarification. It is believed the present changes do not involve any introduction of new matter, whereby entry is in order and is respectfully requested.

In the Official Action, the Examiner made the restriction requirement final and withdrew claims 18-27 from examination on the merits. As claims 18-27 depend directly or indirectly from claim 1, Applicants request rejoinder of non-elected claims 18-27 upon allowance of claim 1.

The Examiner indicated that a sequence listing is required since the specification at least at page 7 discloses several nucleotide sequences in excess of 10 nucleotides. Submitted herewith are computer readable format (CRF) and paper (PDF) copies of the Sequence Listing, together with a Statement of Sequence Listing Identity. It is therefore believed that the sequence listing requirements are fulfilled.

Claim 3 was objected to as containing a misspelling and claims 3-9, 11, 14, 15 and 17 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. This rejection is traversed in view of the amended claims presented herein. Claim 1 recites an oligonucleotide

structure, provides antecedent basis for the terms of the respective dependent claims, including the first and second strands of nucleic acids, and, with the remaining claims, otherwise overcome the various specific objections noted in the Official Action. Accordingly, the claims are definite and the rejection under 35 U.S.C. §112, second paragraph, has been overcome. Reconsideration is respectfully requested.

Claims 1-3, 9-13 and 16 were rejected under 35 U.S.C. §102(e) as being anticipated by the Uhlmann et al U.S. Patent No. 7,615,539, while claims 6-8, 15 and 17 were rejected under 35 U.S.C. §103(a) as being obvious and unpatentable over Uhlmann et al. The Examiner asserted that Uhlmann et al teach a duplexed oligonucleotide, wherein each oligonucleotide is covalently bound to a cholesterol moiety at its terminal ends. The Examiner further asserted that Uhlmann et al further disclose the oligonucleotide comprises a first strand and second strand, with the two strands being hybridized to each other in a duplex section in a manner that a first strand terminal end is not part of the duplex section and is free from a hydrophobic anchoring moiety. With respect to the obviousness rejection, the Examiner asserted that since Uhlmann teaches the use of two lipophilic moieties, following the teaching of an oligonucleotide that has a free region for binding a third strand, it would have been routine optimization with a reasonable expectation of success to determine that the lipophilic moieties should go at the terminal ends.

These rejections are traversed and reconsideration is respectfully requested. Specifically, as defined by clam 1, the present invention is directed to an oligonucleotide structure comprising a first strand of nucleic acid and a second strand of nucleic acid, the first and second strands being hybridized to each other in a duplex section, and at least two hydrophobic anchoring moieties capable of being attached to a lipid membrane. A terminal end of the first strand is not

part of the duplex section and is free from a hydrophobic moiety, and the hydrophobic anchoring moieties are covalently attached to adjacent terminal ends of the first and second strands, respectively.

Uhlmann et al disclose nucleic acid-lipophilic conjugates for modulating an immune response. Uhlmann et al disclose that a duplex forms between two oligonucleotides having partial complementarity wherein at least two nucleotides on each oligonucleotide are capable of base pairing with the other oligonucleotide to enhance activity as the oligonucleotides have minimal or no activity when used alone (see column 18, beginning at line 41). At column 19, examples of SEQ ID NOS: 108 and 109 are shown wherein the 3' ends of the oligonucleotides are substituted with a lipophilic moiety, namely cholesterol. However, it does not appear that the Uhlmann et al duplex includes the lipophilic cholesterol moiety at adjacent terminal ends of the two oligonucleotides as required by claim 1. As described in the present specification, for example at page 2, first full paragraph, the claimed oligonucleotide structures are capable of forming more stable bonds to a lipid membrane and thereby generate an improved control of the process whereby oligonucleotide linkers are introduced to lipid membranes. Accordingly, Uhlmann et al fail to disclose an oligonucleotide structure as recited in claim 1, or claims 2-17 dependent thereon, or the improvements thereof in introducing oligonucleotide linkers to lipid membranes.

Anticipation under 35 U.S.C. §102 requires that each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference. *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999). In view of the failure of Uhlmann et al to teach

an oligonucleotide structure as recited in claim 1, Uhlmann et al fail to anticipate the oligonucleotide structures of claims 1-17.

Further, in determining patentability under 35 U.S.C. §103, it is necessary to determine whether there was an apparent reason to combine the known elements of the prior art in the fashion of the claims at issue, *KSR International Co. v. Teleflex, Inc.*, 550 US 398, 418 (2007). Applicants find no apparent reasoning in the evidence of record that would have led one of ordinary skill in the art to modify the teachings of Uhlmann et al to result in the oligonucleotide structures of claims 1-17. The assertion that it would have been obvious to modify the teachings of Uhlmann et al to provide the lipophilic cholesterol moieties at adjacent terminal ends is simply contrary to the specific teachings of Uhlmann et al. Thus, Uhlmann et al fail to render the oligonucleotide structures of claims 1-17 obvious.

Accordingly, Uhlmann et al do not anticipate or render obvious claims 1-17 and the rejections under 35 U.S.C. §§102 and 103 have been overcome. Reconsideration is respectfully requested.

Finally, claims 1, 2, 4, 9, 10, 12-14 and 16 have been rejected under 35 U.S.C. §102(b) as being anticipated by the Tyagi et al WO 2002/33045. The Examiner asserted that Tyagi et al disclose an oligonucleotide comprising at least two hydrophobic anchoring moieties capable of being attached to a lipid membrane, with the hydrophobic anchoring moieties located on the oligonucleotide terminal ends, which may be adjacent to each other. The Examiner referred to Figure 4 of Tyagi to assert a duplexed oligonucleotide, wherein each oligonucleotide is covalently bound to a cholesterol moiety at its terminal end and the terminal ends having such covalent bonding are adjacent to each other.

This rejection is traversed and reconsideration is respectfully requested. Specifically, as discussed above, the present invention is directed to an oligonucleotide structure comprising a first strand of nucleic acid and a second strand of nucleic acid, the first and second strands being hybridized to each other in a duplex section, and at least two hydrophobic anchoring moieties capable of being attached to a lipid membrane. A terminal end of the first strand is not part of the duplex section and is free from a hydrophobic moiety, and the hydrophobic anchoring moieties are covalently attached to adjacent terminal ends of the first and second strands, respectively.

Tyagi et al discloses oligonucleotide-facilitated coalescence wherein cells, liposomes and lipid particles are provided with respective oligonucleotides. The oligonucleotides are complementary and hybridize to bring the cells, liposomes and/or lipid particles together as an aid to efficient fusion, which may be further aided by asthmatic or electrical shock. Thus, contrary to the oligonucleotide structure of claim 1, comprising both a duplex section and at least two hydrophobic anchoring moieties capable of being attached to a lipid membrane, the respective oligonucleotides of Tyagi et al are each attached to a respective cell, liposome or particle prior to hybridization, rather than being capable of being attached to a cell, liposome or lipid particle in duplex form, as is the oligonucleotide structure of claim 1. Thus, the oligonucleotide structure of claim 1 includes both a duplex section and at least two hydrophobic anchoring moieties capable of being attached to a lipid membrane. On the other hand, the Tyagi et al oligonucleotides are only duplexed after they are attached to cells, liposomes or lipid particles.

As noted, in determining patentability under 35 U.S.C. §103, it is necessary to determine whether there was an apparent reason to combine the known elements of the prior art in the fashion of the claims at issue, *KSR International Co. v. Teleflex, Inc.*, supra. Applicants find no apparent reasoning in the evidence of record that would have led one of ordinary skill in the art to modify the teachings of Tyagi et al to result in the oligonucleotide structures of claims 1-17, including both a duplex section and at least two hydrophobic anchoring moieties capable of being attached to a lipid membrane. Thus, Tyagi et al fail to render the oligonucleotide structures of claims 1-17 obvious, and the rejection under 35 U.S.C. §103 has been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the Official Action and places this application in condition for allowance. In the event that there are any outstanding issues, the Examiner is encouraged to telephone the undersigned in order to expedite their resolution. Please charge any fee required with this response to Deposit Account No. 503915.

Respectfully submitted,

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